CLAIMS

We claim:

1. A targeting construct comprising:
   (a) a first polynucleotide sequence homologous to a CASH gene;
   (b) a second polynucleotide sequence homologous to the CASH gene; and
   (c) a selectable marker.
2. The targeting construct of claim 1, wherein the targeting construct further comprises a screening marker.
3. A method of producing a targeting construct, the method comprising:
   (a) providing a first polynucleotide sequence homologous to a CASH gene;
   (b) providing a second polynucleotide sequence homologous to the CASH;
   (c) providing a selectable marker; and
   (d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.
4. A method of producing a targeting construct, the method comprising:
   (a) providing a polynucleotide comprising a first sequence homologous to a first region of the CASH gene and a second sequence homologous to the CASH gene; and
   (b) inserting a positive selection marker in between the first and second sequences to form the targeting construct.
5. A cell comprising a disruption in a CASH gene.
6. The cell of claim 5, wherein the cell is a murine cell.
7. The cell of claim 6, wherein the murine cell is an embryonic stem cell.
8. A non-human transgenic animal comprising a disruption in a CASH gene.
9. A cell derived from the non-human transgenic animal of claim 8.
10. A method of producing a transgenic mouse comprising a disruption in the CASH gene, the method comprising:
    (a) introducing the targeting construct of claim 1 into a cell;
    (b) introducing the cell into a blastocyst;

(c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse.

11. A method of identifying an agent that modulates the expression or function of CASH, the method comprising:

(a) providing a non-human transgenic animal comprising a disruption in a CASH gene;

(b) administering an agent to the non-human transgenic animal; and

(c) determining whether the expression or function of CASH in the non-human transgenic animal is modulated.

12. A method of identifying an agent that modulates the expression or function of CASH, the method comprising:

(a) providing a cell comprising a disruption in a CASH gene;

(b) contacting the cell with an agent; and

(c) determining whether expression or function of CASH is modulated.

13. An agent identified by the method of claim 11 and claim 12.

14. The non-human transgenic animal of claim 8, wherein the transgenic animal exhibits increased sensitivity to pain.

15. The non-human transgenic animal of claim 8, wherein the transgenic animal exhibits a susceptibility to seizures.

16. A method of identifying an agent that ameliorates pain, the method comprising administering an agent to the non-human transgenic animal of claim 14 and determining whether the agent ameliorates pain in the non-human transgenic animal.

17. A method of evaluating anti-pain treatments, the method comprising administering a therapeutic agent to the non-human transgenic animal of claim 14 and determining the effect of the agent on alleviating pain.

18. A method of identifying an anti-seizure agent, the method comprising administering an agent to the non-human transgenic animal of claim 15 and determining whether the agent has an effect on anti-seizure activity.

19. A method of evaluating anti-seizure treatments, the method comprising administering a therapeutic agent to the non-human transgenic animal of claim 15 and determining the effect of the agent on seizure activity.

20. A transgenic mouse comprising a disruption in a CASH gene, wherein the transgenic mouse exhibits increased sensitivity to pain.

21. A transgenic mouse comprising a disruption in a CASH gene, wherein the transgenic mouse exhibits a susceptibility to seizures.

22. A method of identifying an agent that affects a phenotype associated with a disruption in a CASH gene, the method comprising:

(a) providing a transgenic mouse comprising a disruption in a CASH gene;

(b) administering an agent to the transgenic mouse; and

(c) determining whether agent affects a phenotype in the non-human transgenic animal, wherein the phenotype is increased sensitivity to pain or susceptibility to seizures.

23. A method of identifying an agent that modulates the expression or function of CASH, the method comprising:

(a) providing a transgenic mouse comprising a disruption in a CASH gene;

(b) administering an agent to the transgenic mouse; and

(c) determining whether agent modulates the expression or function;

wherein the agent modulates increased sensitivity to pain or susceptibility to seizures in the transgenic mouse.

24. An agent identified by the method of claim 16, claim 18, claim 22, or claim 23.

25. A method of treating pain, the method comprising administering to a subject in need a therapeutically effective amount of CASH.

26. A method of treating of seizures, the method comprising administering to a subject in need, a therapeutically effective amount of CASH.

27. A pharmaceutical composition comprising CASH.